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INTERNATIONAL COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C. 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 24 October 2000 (24.10.00)	
International application No. PCT/GB00/00860	Applicant's or agent's file reference MGH/PC/P10468PC
International filing date (day/month/year) 09 March 2000 (09.03.00)	Priority date (day/month/year) 09 March 1999 (09.03.99)
Applicant DAVIES, Roger, Wayne et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

29 September 2000 (29.09.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Zakaria EL KHODARY

Telephone No.: (41-22) 338.83.38

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference
(if desired) (12 characters maximum) MGH/PC/P10468PC

Box No. I TITLE OF INVENTION

"NEURODEGENERATIVE DISORDER RELATED GENE"

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

THE UNIVERSITY COURT OF THE UNIVERSITY
OF GLASGOW
Gilbert Scott Building
University Avenue
Glasgow G12 8QQ
UNITED KINGDOM

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (that is, country) of nationality:
GB

State (that is, country) of residence:
GB

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

DAVIES ROGER WAYNE
University of Glasgow, Institute of
Biomedical and Life Sciences
Division of Molecular Genetics
Anderson College, 54 Dumbarton Road
Glasgow G11 6NU, UNITED KINGDOM

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
GB

State (that is, country) of residence:
GB

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☐ agent

☐ common representative

Name and address:

McCALLUM, William Potter; MacDOUGALL, Donald Carmichael; SZCZUKA, Jan Tymoteusz; NAISMITH, Robert Stewart; HORNER, Martin Grenville, SHANKS, Andrew; NEWELL, Campbell; KERR, Sheila Agnes Fife; MORELAND, David; GODWIN, Edgar James; all of
CRUIKSHANK & FAIRWEATHER, 19 ROYAL EXCHANGE SQUARE,
GLASGOW G1 3AE, UNITED KINGDOM (GB)

Telephone No.
0141 221 5767

Facsimile No.
0141 221 7739

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)	
<i>If none of the following sub-boxes is used, this sheet should not be included in the request.</i>	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</i> PAYNE ANTHONY PHILIP University of Glasgow, Institute of Biomedical and Life Sciences West Medical Building, University of Glasgow, University Avenue Glasgow G12 8QQ, UNITED KINGDOM	This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>
State <i>(that is, country)</i> of nationality: GB	State <i>(that is, country)</i> of residence: GB
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</i> SUTCLIFFE ROGER GEORGE University of Glasgow, Institute of Biomedical and Life Sciences, Division of Molecular Genetics, Anderson College, 54 Dumbarton Road Glasgow G11 6NU, UNITED KINGDOM	This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>
State <i>(that is, country)</i> of nationality: GB	State <i>(that is, country)</i> of residence: GB
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</i> 	This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>
State <i>(that is, country)</i> of nationality:	State <i>(that is, country)</i> of residence:
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)</i> 	This person is: <input type="checkbox"/> applicant only <input type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only <i>(If this check-box is marked, do not fill in below.)</i>
State <i>(that is, country)</i> of nationality:	State <i>(that is, country)</i> of residence:
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<input type="checkbox"/> Further applicants and/or (further) inventors are indicated on another continuation sheet.	

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- ☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|--|--|
| <input checked="" type="checkbox"/> AE United Arab Emirates | <input checked="" type="checkbox"/> LR Liberia |
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LS Lesotho |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LT Lithuania |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MA Morocco |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BR Brazil | |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> CR Costa Rica | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> DM Dominica | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GD Grenada | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GM Gambia | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> HR Croatia | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> TZ United Republic of Tanzania |
| <input checked="" type="checkbox"/> ID Indonesia | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IN India | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> IS Iceland | |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | <input checked="" type="checkbox"/> ZA South Africa |
| | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KR Republic of Korea | Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet: |
| <input checked="" type="checkbox"/> KZ Kazakhstan | <input type="checkbox"/> |
| <input checked="" type="checkbox"/> LC Saint Lucia | <input type="checkbox"/> |
| <input checked="" type="checkbox"/> LK Sri Lanka | |

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

Box No. VI PRIORITY CLAIM		<input type="checkbox"/> Further priority claims are indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application: regional Office	international application: receiving Office
item (1) 9 MARCH 1999	GB9905218.5	UNITED KINGDOM		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (1)

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(iii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA/

Request to use results of earlier search: reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day-month-year)

Number

Country (or regional Office)

Box No. VIII CHECK LIST: LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 4
description (excluding sequence listing part) : 50
claims : 7
abstract : 1
drawings : 26
sequence listing part of description :
Total number of sheets : 88

This international application is accompanied by the item(s) marked below:

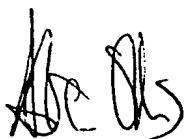
1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☐ other (specify):

Figure of the drawings which should accompany the abstract:

Language of filing of the international application:

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).



A. SHANKS.

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings: <input type="checkbox"/> received: <input type="checkbox"/> not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA/	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MGH/PC/P10468PC		FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/GB 00/ 00860	International filing date (day/month/year) 09/03/2000	(Earliest) Priority Date (day/month/year) 09/03/1999
Applicant THE UNIVERSITY COURT OF THE UNIVERSITY OF GLASGOW		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.
☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- ☐ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.
- ☒ None of the figures.

INTERNATIONAL SEARCH REPORT

National Application No

PCT/GB 00/00860

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/45 A61K48/00 A61K39/395 C12N9/12 C12N15/54
A01K67/027 C07K16/40 C12Q1/48 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C12N A01K C07K C12Q A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ABELOVICH, A. ET AL: "Modified hippocampal long-term potentiation in PKCgamma-mutant mice" CELL, vol. 75, 31 December 1993 (1993-12-31), pages 1253-1262, XP000910293 "results" on page 1254 with reference to "Generation of PKCgamma-mutant mice"	32,33
X	WO 95 02069 A (BENNETT C FRANK ;BOGGS RUSSELL T (US); DEAN NICHOLAS M (US); ISIS) 19 January 1995 (1995-01-19) page 3, line 20 - line 21 page 5, line 21 - line 33 page 13, line 6 - line 9 table 5 ----- -/--	36

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"G" document member of the same patent family

Date of the actual completion of the international search

26 June 2000

Date of mailing of the international search report

24/07/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Pilling, S

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE WPI Section Ch, Week 199444 Derwent Publications Ltd., London, GB; Class B05, AN 1994-354659 XP002140960 & JP 06 279311 A (NIPPON SHOJI KK), 4 October 1994 (1994-10-04) abstract</p> <p>---</p>	37
X	<p>KOLB, H. ET AL: "Differential staining of neurons in the human retina with antibodies to protein kinase C isozymes" VISUAL NEUROSCIENCE, vol. 10, 1993, pages 341-351, XP000915830 abstract</p> <p>---</p>	38-41
X	<p>CAZAUBON, S. ET AL: "Effector dependant conformational changes in protein kinase C-gamma through epitope mapping with inhibitory monoclonal antibodies" EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 194, 1990, page 799-804 XP002109461 abstract</p> <p>---</p>	38-41
X	<p>CAZAUBON, S. ET AL: "Monoclonal antibodies to protein kinase C-gamma: functional relationship between epitopes and co-factor binding sites" EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 182, 1989, pages 401-406, XP000915810 abstract</p> <p>---</p>	38-41
X	<p>SMALLWOOD, J. I. ET AL: "An apparently novel protein of human leukocytes, reactive with an antibody to protein kinase C-gamma, is rapidly modified upon cell activation: Initial characterization in neutrophils and their cytoplasts" INFLAMMATION, vol. 22, no. 1, February 1998 (1998-02), pages 1-28, XP000915851 abstract</p> <p>---</p>	38-41
A	<p>WO 98 39444 A (INCYTE PHARMA INC ;HILLMAN JENNIFER L (US)) 11 September 1998 (1998-09-11) page 2, line 10 -page 2, line 13 page 22, line 7 - line 10</p> <p>---</p> <p style="text-align: center;">-/--</p>	1-44

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	FAVIT, A. ET AL: "Alzheimer's-specific effects of soluble beta-amyloid on protein kinase-C-alpha and gamma degradation in human fibroblasts" PROC. NAT. ACAD. SCI. USA, vol. 95, 12 May 1998 (1998-05-12), pages 5562-5567, XP000901213 the whole document ---	1-44
A	SHIMOHAMA, SHUN ET AL: "Signal transduction mechanisms in Alzheimer disease" ALZHEIMER DISEASE AND ASSOCIATED DISORDERS, vol. 9 (SUPP 2), 1995, pages 15-22, XP000915805 the whole document ---	1-44
A	CRAIG, N. J. ET AL: "Genetic and physical mapping of the agu mutation." SOCIETY FOR NEUROSCIENCE ABSTRACTS, (1997) VOL. 23, NO. 1-2, PP. 1873. MEETING INFO.: 27TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE NEW ORLEANS, LOUISIANA, USA OCTOBER 25-30, 1997 , XP000915938 abstract -----	1-44

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00860

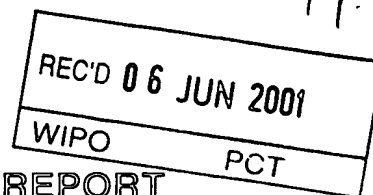
Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9502069	A	19-01-1995	US 5681747 A	28-10-1997
			US 5703054 A	30-12-1997
			AU 710972 B	30-09-1999
			AU 7007198 A	30-07-1998
			AU 688354 B	12-03-1998
			AU 7398194 A	06-02-1995
			BR 9406931 A	10-09-1996
			CA 2166058 A	19-01-1995
			EP 0714449 A	05-06-1996
			FI 960089 A	07-03-1996
			HU 75834 A	28-05-1997
			JP 8507929 T	27-08-1996
			NO 960079 A	29-02-1996
			NZ 269653 A	19-12-1997
			US 6015892 A	18-01-2000
			US 5882927 A	16-03-1999
			US 5959096 A	28-09-1999
			US 5916807 A	29-06-1999
			US 5885970 A	23-03-1999
			US 5948898 A	07-09-1999
			US 5922686 A	13-07-1999
<hr/>				
JP 6279311	A	04-10-1994	NONE	
<hr/>				
WO 9839444	A	11-09-1998	US 5922571 A	13-07-1999
			AU 6544198 A	22-09-1998
			EP 0981615 A	01-03-2000
			US 6015678 A	18-01-2000
<hr/>				

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference PC/SJB/P10468PC	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/00860	International filing date (day/month/year) 09/03/2000	Priority date (day/month/year) 09/03/1999
International Patent Classification (IPC) or national classification and IPC A61K38/45		
Applicant THE UNIVERSITY COURT OF THE UNIVERSITY OF GLASGOW		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 29/09/2000	Date of completion of this report 01.06.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Pilling, S Telephone No. +49 89 2399 8461



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/00860

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
Description, pages:

1-50 as originally filed

Claims, No.:

1-32 as originally filed

33-43 as received on 02/03/2001 with letter of 28/02/2001

Drawings, sheets:

1/26-26/26 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

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- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-36,38-43
	No:	Claims	37
Inventive step (IS)	Yes:	Claims	1-36,38-43
	No:	Claims	37
Industrial applicability (IA)	Yes:	Claims	1-43
	No:	Claims	

- 2. Citations and explanations**
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

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Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The documents cited in the International Search Report (ISR) are consecutively numbered D1 to D11 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.

Claims 1 to 17, 34 and 35; uses of a PKC γ polynucleotide/PKC type 1 polypeptide for treating neurodegenerative disorders

2. None of the documents cited in the present search report disclose the use of a PKC γ polynucleotide/PKC type 1 polypeptide for treating neurodegenerative disorders.
3. Thus, the subject matter of Claim 1 to 17, 34 and 35 is new (Article 33(2) PCT).
4. Document D3 describes that activators of protein kinase C isozymes may be used to treat Alzheimer's disease while document D8 discloses inhibitors of protein kinase C for the treatment Alzheimer's disease. Hence the teaching of these documents appears to be contradictory. On turning to experimental studies of the mechanism underlying Alzheimer's disease, although the role of PKC γ has been studied (see D9 or D10), no clear causal relationship appears to have been established. Moreover, with reference to the mutant AGU rat strain described in the present description, it appears that PKC γ had not been identified as the site of the AGU mutation (see document D11). Hence, in light of the inconclusive and conflicting teaching of the prior art, it appears that it would not have been obvious for the skilled man to use a PKC γ polynucleotide or a PKC type 1 polypeptide for treating neurodegenerative disorders.
5. Thus, the subject matter of Claims 1 to 17, 34 and 35 is inventive (Article 33(3) PCT).

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Claims 18 to 31; methods of testing animals for neurodegenerative disorders

6. None of the documents cited in the present search report disclose methods of testing animals for neurodegenerative disorders by detecting mutations in the PKC γ gene.
7. Thus, the subject matter of Claim 18 to 31 is new (Article 33(2) PCT).
8. For reasons similar to those outlined herein above, in view of the inconclusive and conflicting nature of the prior art, it does not appear to have been obvious that neurodegenerative disorders such as Alzheimer's disease are caused by mutation(s) in PKC γ . Thus, the skilled man would not have been motivated to test animals for neurodegenerative disorders by detecting mutations in the PKC γ gene and the subject matter of Claims 18 to 31 is inventive (Article 33(3) PCT).

Claims 32 and 33; uses of a truncated PKC γ polynucleotide/PKC type 1 polypeptide for producing animal models

9. None of the documents cited in the present search report disclose the use of a truncated PKC γ polynucleotide/PKC type 1 polypeptide for promoting nervous system degeneration for producing animal models. Thus, the subject matter of Claims 32 and 33 is new (Article 33(2) PCT).
10. Document D1 describes the use of a homologous recombination vector comprising the PKC γ sequence with a 2.5 kb deletion (rather than a truncation) to create transgenic animal models useful for studying the role of kinases in learning and memory. In contrast to the transgenic animals of document D1, however, the present transgenic animals display neurodegeneration, *i.e.* an obvious movement disorder and abnormalities in brain structure. This latter effect associated with the use of truncated PKC γ polynucleotide/PKC type 1 polypeptide could not have apparently been predicted on the basis of document D1.
11. Thus, the subject matter of Claims 32 and 33 is inventive (Article 33(3) PCT).

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Claim 36: polynucleotide fragments encoding PKC type 1 polypeptide for use in gene therapy

12. None of the documents cited in the ISR disclose polynucleotide fragments encoding PKC type 1 polypeptide for use in gene therapy. Hence, the subject matter of Claim 36 appears to be new.
13. Although, document D2 describes anti-sense therapy of diseases using oligonucleotides directed towards PKC γ , it appears that these short nucleotide sequences of approximately 20 bp length would not encode the entire PKC type I polypeptide. In the absence of any suggestion or teaching in this document towards the use of longer fragments as defined in present Claim 36, it appears that, the subject matter of Claim 36 is inventive (Article 33(3) PCT).

Claim 37: uses of PKC type 1 polypeptides for identification of compounds for treating neurodegenerative disorders

14. Document D3 describes the production of activators of PKC γ and their use to treat "*senile dementia accompanied with central nerve disorder, esp. Alzheimer's diseases*". Hence, although the scope of Claim 37 is unclear (see "Re Item VIII" herein below), it appears that document D3 discloses the use of PKC γ (type I) polypeptides to identify activators thereof for the treatment of neurodegenerative disorders.
15. Thus, as far as can presently be determined, the subject matter of Claim 37 is not new (Article 33(2) PCT).

Claims 38 to 43: antibodies specific for PKC γ derived polypeptides and uses thereof

16. None of the documents cited in the present search report suggests or points towards humanised monoclonal antibodies specific for PKC γ derived polypeptides or the use of antibodies specific for PKC γ derived polypeptides to treat degeneration of the nervous system or in a diagnostic assay for a neural degenerative disorder. Thus, the subject matter of Claims 38 to 43 is new and

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inventive (Article 33(2) PCT).

Re Item VIII

Certain observations on the international application

17. Claim 37 defines the "*use of a PKC γ type 1 polypeptide for the identification of compounds for use in the treatment of neurodegenerative disorders*" and is unclear because this claim fails to define how said "*PKC γ type 1 polypeptide*" is used to identify compounds for use in the treatment of neurodegenerative disorders (Article 6 PCT). Furthermore this claim is considered to be unduly broad and speculative (Article 6 PCT) since the description fails to clearly exemplify the identification of any new therapeutic compounds.

33. Use of a truncated PKC type I polypeptide for promoting nervous system degeneration for the production of animal models.

34. Use of a PKC γ polynucleotide fragment encoding the
5 PKC type I polypeptide in the manufacture of a medicament for preventing, delaying, treating or inhibiting degeneration of nervous system.

35. Use of a PKC type I polypeptide in the manufacture
10 of a medicament for preventing, delaying, treating or inhibiting degeneration of nervous system.

36. A polynucleotide fragment encoding the PKC type I polypeptide for use in gene therapy.
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37. Use of a PKC γ type I polypeptide for the identification of compounds for use in the treatment of neurodegenerative disorders.

20 38. A humanised monoclonal antibody specific for an epitope(s) located on a truncated polypeptide produced from the PKC γ gene.

25 39. An antibody according to claim 38 wherein the epitope(s) is/are located in the C terminal half of the PKC type I polypeptide.

40. An antibody according to claim 42 wherein the C terminal half of the polypeptide begins at amino acid number 282 and ends at the C terminus of the native polypeptide.

41. An antibody according to any of claims 38 to 40
5 wherein the antibody is a monoclonal antibody.

42. Use of an antibody according to claims 38 - 41 for the manufacture of a medicament for preventing, delaying, treating or inhibiting degeneration of the nervous system.

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43. Use of an antibody according to claims 38 - 41 in a diagnostic assay for testing an human thought to have or be predisposed to having a neural degenerative disorder.

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MC

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing

(day/month/year)

01.06.2001

Applicant's or agent's file reference

PC/SJB/P10468PC

IMPORTANT NOTIFICATION

International application No.

PCT/GB00/00860

International filing date (day/month/year)

09/03/2000

Priority date (day/month/year)

09/03/1999

Applicant

THE UNIVERSITY COURT OF THE UNIVERSITY OF GLASGOW

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

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